**Contribution of Elastin to Cardiovascular Development in Zebrafish**

Elastin is as an extracellular protein that allows tissues in vertebrates to extend and recoil. It is synthesized early in life and has a long half-life. Heterozygous loss of function mutations in the elastin gene, cause the disease supravalvular aortic stenosis (SVAS), a progressive arterial obstructive disease which can cause hypertension, and even heart failure. The focus of this research is to understand the developmental and molecular mechanisms of this disease using an animal model by targeting the likely zebrafish paralogs of elastin, *elna* and *elnb*.

First, we analyzed the genomic and transcript diversity of *elna* and *elnb* using publicly available sequence data as well as sequencing of RT-PCR products. All available zebrafish *eln* transcipts were collected and aligned with each other and to the available genomic sequences using the CLC Main software. Most alternative splicing events and length variants were observed within the last 20 exons. As similar observations were made in the human *ELN* gene, we propose that extensive length variation is an evolutionarily conserved feature of vertebrate elastin genes, producing a large ensemble of protein isoforms.

To understand the contribution of elastin in zebrafish development, we performed antisense morpholino oligonucleotide knockdown experiments. Following either *elna* or *elnb* knockdown, we observed reduced embryo length, curved tails, pericardiac edema, arrhythmia and bradycardia, pooling of blood and reduced blood flow throughout the vessels.  The embryo also displayed deformed or underdeveloped jaws and elongated malformed hearts.  Even with these changes in phenotype, there was no significant decrease in survival up to 5 days post-fertilization. In addition, we established an elna mutant (sa12235, p.Y88\*) line, which displays similar cardiac defects to the elna morphants. Future work will focus on generating an *elnb* mutant using CRISPR/Cas9 genome editing, examining the cardiovascular phenotypes and associated molecular changes in the mutants and rescuing the mutant phenotypes by mRNA injections and pharmacological treatment.